

## AMENDMENTS TO THE SPECIFICATION

1. Please amend paragraph [0071] on page 25 as follows:

**Figure 27** depicts an overview of multidimensional chemical genetic analysis. **(A)** The three part protocol involved in screening of 7,392 diversity-oriented synthesis-derived deacetylase inhibitors. Chemical genetic information is obtained as 'object-observations' and arranged in a matrix, denoted by  $S$ . Each column ( $y_j$ ) in  $S$  is a descriptor which corresponds to a phenotype from a cell-based or biochemical assay. Each row ( $x_i$ ) in  $S$  is an object which corresponds to a chemical. An element ( $m, n$ ) of  $S$ , encodes information about chemical  $m$  for descriptor  $n$ . [ITSA1 is a chemical genetic modifier that suppresses TSA-induced histone and  $\alpha$ -tubulin acetylation; See, for example, Koeller, K.M., Haggarty, S.J., Perkins, B.D., Leykin, I., Wong, J.C., Kao, M.C., and Schreiber, S.L. (2003). Chemical Genetic Modifier Screens: small molecule trichostatin suppressors as probes of intracellular histone and tubulin acetylation. *Chem. Biol.* 10(5):397-410]. **(B)** Summary of small molecules based upon a 1,3-dioxane structure and combinatorics of the full library. **(C)** ~~Structure of ITSA1, a chemical genetic modifier that suppresses TSA induced histone and  $\alpha$  tubulin acetylation [Koeller, K.M., Haggarty, S.J., Perkins, B.D., Leykin, I., Wong, J.C., Kao, M.C., and Schreiber, S.L. (2003). Chemical Genetic Modifier Screens: small molecule trichostatin suppressors as probes of intracellular histone and tubulin acetylation. *Chem. Biol.* 10(5):397-410].~~ **(D)** Summary of screens performed and abbreviations used for the assays.

2-. Please amend paragraph [0478] beginning on page 154 and ending on page 155 as follows:

A summary of the cell-based assays performed is shown in ~~Fig. 27D~~ Fig. 27C. Following robotic pin-transfer [Walling, L.A., Peters, N.R., Horn, E.J., and King, R.W. (2001). New technologies for chemical genetics. *J. Cell Biochem. Suppl.* 37, 7-12], the 1,3-dioxane-based small molecules (~2-5  $\mu$ M depending upon efficiency of synthesis and amount of compound pin-transferred) were incubated with cells for a total of 18 hours. The entire collection of 7,392 molecules was screened (in duplicate) in the AcTubulin and AcLysine cyto blot assays (e.g., (Fig. 28A)). A subset of the library was then further evaluated in three other acetylation-based assays,

including one involving the suppressor ITSA1. Correlation between replicates was strong, with  $r = 0.84$  ( $p\text{-value} < 0.05$ ) representing the minimum correlation between duplicate plates containing hydroxamic acids (Fig. 28B). Values from replicates were standardized to a control from each plate, averaged, and  $\text{Log}_2$ -transformed to reduce the skewness and kurtosis prior to fitting to a normal distribution. Statistical properties pertaining to each  $\mathbf{R}'$  biasing element (*i.e.*, metal chelator) in the library are shown in the box-plots in Fig. 28C. Since diversity position  $\mathbf{R}'$  was encoded spatially, as well as by tagging, we were able to determine the relative distribution of bioactive small molecules amongst the three biasing elements. Under the assumption of equal synthetic efficiency and purity, the hydroxamic acids were assessed to be most active and the *o*-aminoanilides least active in both the AcTubulin and AcLysine assays (Fig. 28D).